

Figure 1

100
General Process for Developing and Implementing
a Regulated Biochemical Reaction Network Model

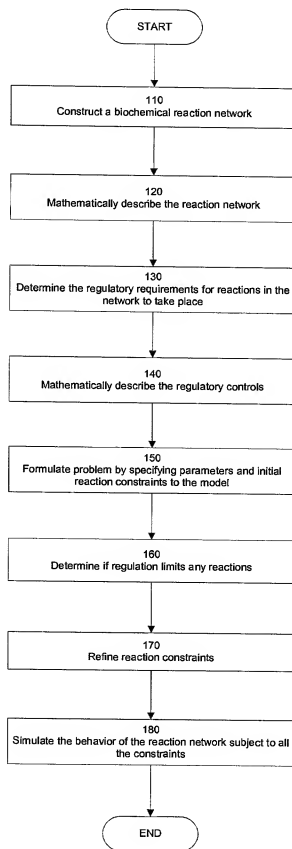
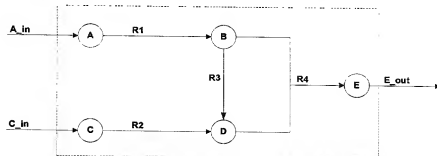


Figure 2

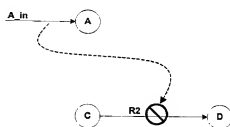
A)

Example Biochemical Reaction Network



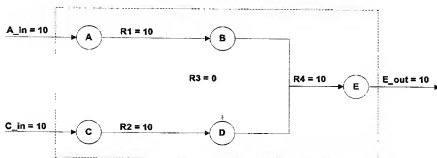
B)

Example Regulatory Structure and Requirements



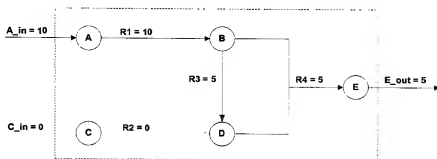
C)

Simulated Reaction Network (without regulation)



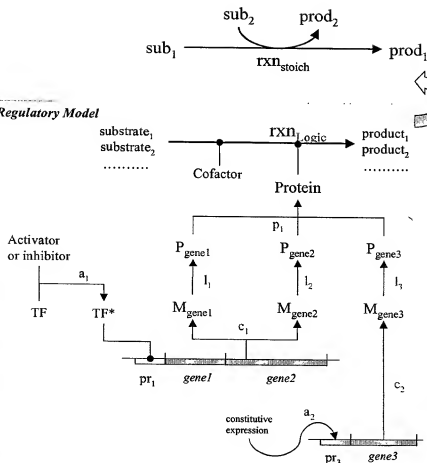
D)

Simulated Reaction Network (with regulation)



[illegible]

Regulatory Model



- **Activity constraints set for rxn_{stoch}**
(lower bound = 0, upper bound = ∞ or #)
- **Inactivity constraints for rxn_{stoch}**
(lower bound = 0, upper bound = 0)

Integration of Stoichiometric model and Logical model achieved through regulatory restraints (logic values of reaction processes) which are used to refine appropriate reaction constraints in the model:

If $\text{rxn}_{\text{Logic}} = 1$ then use Activity constraints

If $\text{rxn}_{\text{Logic}} = 0$ then use Inactivity constraints

Logic functions

$$a_1 = (\text{activator/inhibitor}) \cdot \text{TF}$$

$$a_2 = 1$$

$$c_1 = \text{TF}^* \cdot \text{pr}_1 \cdot \text{gene1} \cdot \text{gene2}$$

$$c_2 = pr_3 \cdot gene3$$

$$I_1 = M_{\text{scnd}}$$

$$I_2 = M_{\text{gen}2}$$

$$I_3 = M_{\text{генс3}}$$

$$p1 = P_{\text{gene1}} \cdot P_{\text{gene2}} \cdot P_{\text{gene3}}$$

$$\text{rxn}_{\text{Logic}} = \text{Protein} \cdot \text{Cofactor} \cdot \text{Substrate}_1 \cdot \text{Substrate}_2$$

Time delays can be specified for the switching of each memorization variable after a triggering change in the associated function

Figure 4

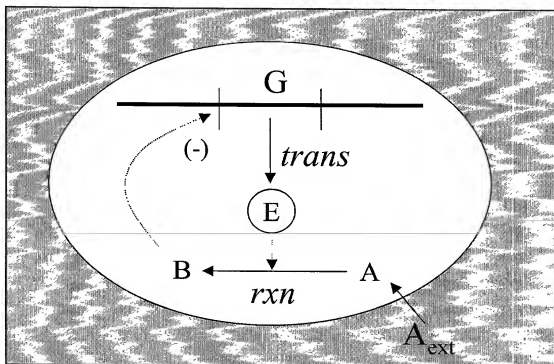


Figure 5

200

A Time-Dependent Implementation of a Regulated
Biochemical Reaction Network Model

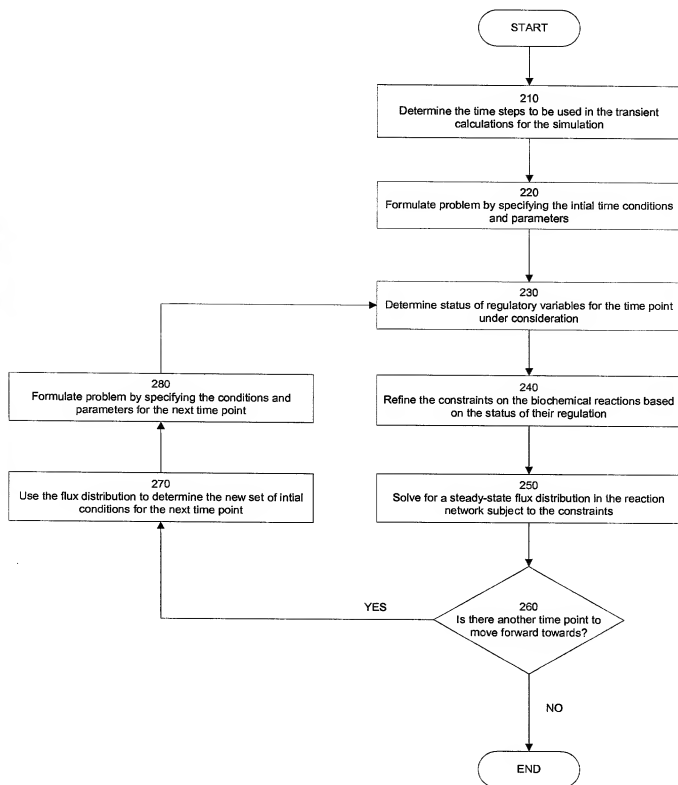


Figure 6

300 Process for Developing Genome Scale Regulated Models of Metabolism

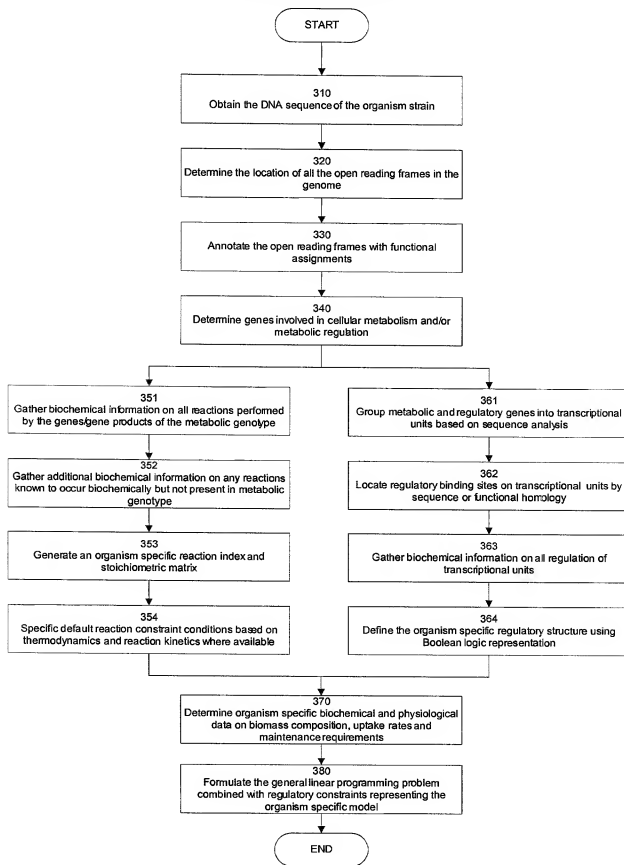
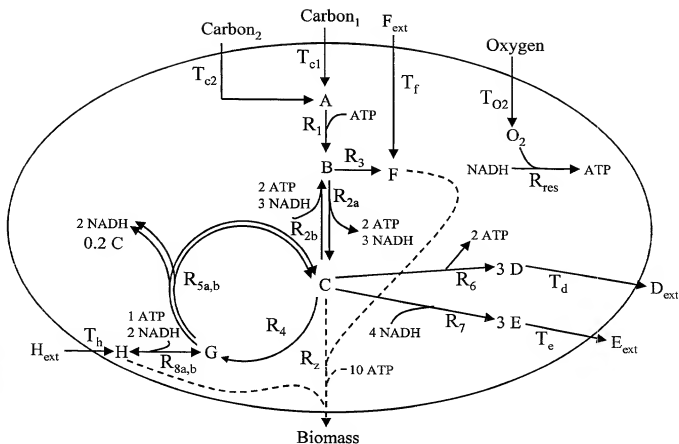


Figure 7



REACTION	NAME	REGULATION
<i>Metabolic Reactions</i>		
-1 A -1 ATP +1 B	R1	
-1 B +2 ATP +2 NADH +1 C	R2a	IF NOT(RPb)
-1 C -2 ATP -2 NADH +1 B	R2b	
-1 B +1 F	R3	
-1 C +1 G	R4	
-1 G +0.8 C +2 NADH	R5a	IF NOT(RPo2)
-1 G +0.8 C +2 NADH	R5b	IF RPo2
-1 C +2 ATP +3 D	R6	
-1 C -4 NADH +3 E	R7	IF NOT(RPh)
-1 G -1 ATP -2 NADH +1 H	R8a	IF NOT(RPh)
+1 G +1 ATP +2 NADH -1 H	R8b	
-1 NADH -1 O ₂ +1 ATP	Rres	IF NOT(RPo2)
<i>Transport Processes</i>		
-1 Carbon1 +1 A	Tc1	
-1 Carbon2 +1 A	Tc2	IF NOT(RPc1)
-1 Fext +1 F	Tf	
-1 D +1 Dext	Td	
-1 E +1 Eext	Te	
-1 Hext +1 H	Th	
-1 Oxygen +1 O ₂	To2	
<i>Maintenance/Growth Processes</i>		
-1 C -1 F -1 H -10 ATP +1 Biomass	Growth	
<i>Regulatory Proteins</i>		
	RPo2	IF NOT(Oxygen)
	RPc1	IF Carbon1
	RPh	IF Th
	RPb	IF R2b

Figure 8

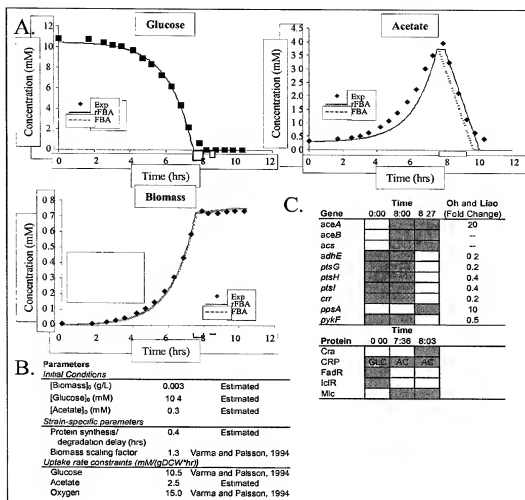


Figure 9

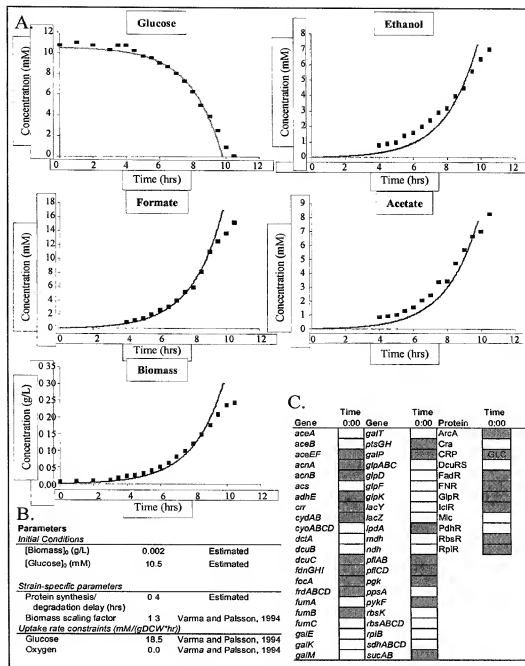


Figure 10

